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APPLICATION NUMBER: ***60/465,134***
FILING DATE: ***April 24, 2003***
RELATED PCT APPLICATION NUMBER: *PCT/US04/12758*

By Authority of the
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04-25-03

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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Rinat O.	**Esenaliev**	**Galveston, TX**
Donald S.	**Prough**	**Galveston, TX**

☐ *Additional inventors are being named on the __ separately numbered sheets attached hereto*

TITLE OF THE INVENTION (280 characters max)

NONINVASIVE BLOOD ANALYSIS BY OPTICAL PROBING OF THE VEINS UNDER THE TONGUE

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ENCLOSED APPLICATION PARTS (*check all that apply*)

☒ Specification 8 ☐ CD(s), Number

☒ Sheet of Drawings 3 ☒ Other (specify) Postcard

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☒ Applicant claims small entity status. See 37 CFR 1.27.
☒ A check or money order is enclosed to cover the filing fees.
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The invention was made by an agency of the United States Government or under a contract with an agency of the Uni States Government.
☒ No
☐ Yes, the name of the U.S. Government agency and the Government contract number are:______

Respectfully submitted,

SIGNATURE ______ Date: 24 Ap

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EV 358 855 864 US — CERTIFICATION UNDER 37 C.F.R. § 1.10 — 24 April 2003
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I hereby certify that this Application and the documents referred to as enclosed therein are being deposited with the United States Postal Service in an envelope as "Express Mail Post Office to Addressee" addressed to:

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Robert W. Strozier — 24 April 2003
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Honorable Commissioner for Patents
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Washington, D.C. 20231-9999

Attorney Docket No.
98006/26PRV

Re: **US PSN: 60/ ; FD:23 April 2003**
Title: NONINVASIVE BLOOD ANALYSIS BY OPTICAL PROBING OF THE VEINS UNDER THE TONGUE
Our Ref. No.: 98006/26PRV

Dear Sir/Madam:

This letter is a request to file a **Provisional Patent Application** including: **(1) a 8 pa disclosure; (2) 3 sheets of drawings; (3) Transmittal Small Entity; and (4) a Return Recei Postcard.**

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UNITED STATES PROVISIONAL PATENT APPLICATION

TITLE: **NONINVASIVE BLOOD ANALYSIS BY OPTICAL PROBING OF TH VEINS UNDER THE TONGUE**

INVENTOR: Rinat O. Esenaliev and Donald S. Prough

ASSIGNEE: Board of Regents of the University of Texas System

BACKGROUND OF THE INVENTION

1. Field of the Invention

[0001] The present invention relates to a novel system and method for non-invasive analysis blood including blood components and analytes.

[0002] More particularly, the present invention relates to a novel system and method for no invasive analysis of blood including blood components and analytes, where the system is a portat and pocket-sized and includes a probe having a tip designed to be placed in proximity to or in dire contact with a tissue over a big vein of an underside of a patient's tongue, where the tip includes excitation port through which an input signal generated by a signal generator subsystem imping on a surface of a tissue over the vein and a response port through which a response signal is receiv by and forwarded to a detector and analyzer or a detector/analyzer, which converts the respon signal into concentration of a blood component and/or a value of a blood parameter.

2. Description of the Related Art

[0003] Analysis of blood is needed for diagnostic and management of various diseases a conditions as well as for screening of healthy population. Current techniques and systems for blo analysis are invasive, require blood sampling, and cannot be performed in real time or continuous At present, blood is usually analyzed in clinical laboratories after taking blood samples with invasi techniques.

[0004] Thus, there is a need in the art for a technique and system for noninvasive analysis of blo that would benefit a large population of patients and healthy people as well.

SUMMARY OF THE INVENTION

[0005] The present invention provides a system for non-invasive analysis of blood including a prc having a tip designed to be placed in proximity to or in direct contact with a tissue over a big v of an underside of a patient's tongue, where the tip includes an excitation port through which input signal generated by a signal generator subsystem impinges on a surface of the tissue over vein and a response port through which a response signal is received by and forwarded to a detec

and analyzer or a detector/analyzer, which converts the response signal into concentration of a bloc component and/or a value of a blood parameter.

[0006] The present invention also provides a portable and pocket-sized system for non-invasi analysis blood including a probe having a tip designed to be placed in proximity to or in dire contact with a tissue over a big vein of an underside of a patient's tongue, where the tip includes a excitation port through which an input signal generated by a signal generator subsystem imping on a surface tissue over the vein and a response port through which a response signal is received l and forwarded to a detector and analyzer or a detector/analyzer, which converts the response sign into concentration of a blood component and/or a value of a blood parameter.

[0007] The present invention also provides a system including an excitation signal generator, probe including a tip designed to be placed in proximity to or in contact with a tissue over a big ve of an underside of a patient's tongue and having an excitation signal port connected to the generat via a signal transmission conduit and a response port connected to a detector which is in tu connected to an analyzer or a detector analyzer, where the analyzer converts the response signal in a concentration of a blood component and/or a value of a blood parameter.

[0008] The present invention also provides a portable and pocket-sized system for non-invasi glucose and/or cholesterol measuring and monitoring including a probe having a tip designed to placed in proximity to or in direct contact with a tissue over a big vein of an underside of a patien tongue, where the tip includes an excitation port through which an input signal generated by a sign generator subsystem impinges on a tissue surface over the vein and a response port through whi a response signal is received by and forwarded to a detector and analyzer or a detector/analyz which converts the response signal into concentrations of a glucose and/or cholesterol in the bloc

[0009] The present invention also provides a portable and pocket-sized system for non-invasi hemoglobin, hematocrit, oxy-hemoglobin, deoxy-hemoglobin, carboxyhemoglobin, and glycosylated or glycated hemoglobin measuring and monitoring including a probe having a designed to be placed in proximity to or in direct contact with a tissue over a big vein of underside of a patient's tongue, where the tip includes an excitation port through which an in signal generated by a signal generator subsystem impinges on a tissue surface of the vein an response port through which a response signal is received by and forwarded to a detector a analyzer or a detector/analyzer, which converts the response signal into concentrations hemoglobin, hematocrit, oxy-hemoglobin, deoxy-hemoglobin, carboxyhemoglobin, and glycosylated or glycated hemoglobin in the blood.

[0010] The present invention provides a method for measuring and/or monitoring blood componen and/or parameters including the steps of placing a tip of a probe having an excitation port and response port in proximity to or in direct contact with a tissue over a big vein of an underside of patient's tongue. Once the tip is in proximity to or in contact with the tissue over the vei transmitting an excitation signal into the vein through the excitation port, where the excitation sign is generated by a signal generator connected to the excitation port of the probe via a sign transmission conduit. After the excitation signal or input signal is transmitted into the vei receiving a response signal through the response port and detecting the response signal in a detectc

[0011] The present invention provides a method for measuring and/or monitoring blood componen and/or parameters including the steps of placing a tip of a probe having an excitation port and response port in proximity to or in direct contact with a tissue over a big vein of an underside oi patient's tongue. Once the tip is in proximity to or in contact with the tissue over the vei transmitting an excitation signal into the vein through the excitation port, where the excitation sign is generated by a signal generator connected to the excitation port of the probe via a sign transmission conduit. After the excitation signal or input signal is transmitted into the vei receiving a response signal through the response port directly into a detector which generates detector signal which is transmitted via a detector signal conduit to an analyzer or via a respon signal conduit to a detector/analyzer. Once the signal has been detected, the analyzer converts t detected signal into a concentration of a blood component and/or a value of a blood parameter.

DESCRIPTION OF THE DRAWINGS

[0012] The invention can be better understood with reference to the following detailed descripti together with the appended illustrative drawings in which like elements are numbered the same

[0013] Figures 1A-C depict three preferred embodiments of apparatuses of this invention.

DETAILED DESCRIPTION OF THE INVENTION

[0014] The inventor has found that a novel system and method for non-invasive analysis of blo including blood components and analytes can be constructed and used. Portable, pocket-siz devices can be developed for home and clinical use based on this technique permitting wi application for the apparatuses of this invention.

[0015] The technique is based on optical analysis of blood circulating in a big vein under a patie tongue. Light from an optical probe of an apparatus of this invention is directed into one of th veins via brining a probe tip in close proximity to or in contact with a surface of tongue tissue abc the vein, *i.e.*, the tip of the probe is brought into proximity to or in contact with some epithe

tissue on the underside of the tongue with the big vein beneath. Non-contact analysis may ultimately be the preferred method from a medical and practical point of view because the tip does not make contact with the tissue reducing the possibility of infections. The emitted light interacts with blood flowing through the vein, producing a signal. The produced or output signal is received or received and measured by the probe, where the output signal will depend on optical properties of the blood. The optical properties of the blood are related to concentrations of blood components. Because the tissues between the probe tip and blood circulating in the vein is very thin, the output signals received by the apparatuses of this invention have minimal influences from the intervening tissue (*i.e.*, minimal background signals) caused by light scattering and absorption in the intervening tissue.

[0016] The term "in proximity to" means that the probe tip is sufficiently close to the surface tissue of the underside of the tongue of a patient to produce a response signal of sufficient intensity to be measured. Generally, the distance is between about 10 mm and about 1mm, with distances between about 5 mm and 1 mm being preferred. However, larger or smaller distances can be used as well provided an analyzable signal can be detected. The term "in contact with" means that the probe tip actually makes physical contact with the tissue of the underside of the patient's tongue.

[0017] The excitation light can be in the near infrared (wavelength range from about 760 to about 2,500 nm), the visible (wavelength range from about 400 to about 760 nm), or the near UV (from about 250 to about 400 nm) portions of the electromagnetic spectrum. These portions of the electromagnetic spectrum would have insignificant background signals due to relatively low scattering and absorption in the intervening tissue compared with light from other spectral ranges

[0018] The method and system of this invention can utilize any optical detection technique or hybri detection techniques including, but not limited to, reflectance techniques, confocal techniques scanning confocal techniques, polarization techniques, interferometry techniques, optoacousti techniques, low coherence reflectometry techniques, techniques based on speckle measurement or similar techniques or mixtures or combinations thereof.

[0019] One preferred application of this invention is noninvasive measurement of hemoglobi concentration and/or hematocrit in blood. Other applications of the systems and methods of th invention include, without limitation, noninvasive measurements of glucose and/or cholester concentrations in blood and potentially be used for measuring oxy-, deoxy-, carboxyhemoglobi and/or glycosylated hemoglobin concentrations in blood. Other applications include, witho limitation, measuring or monitoring analytes, drugs, exogenous substances, and/or blood paramete

(such as pH).

[0020] This technique can be used for blood analysis of healthy population and patients with various diseases and disorders including critically ill patients.

[0021] Referring now to **Figures 1A-C**, a preferred embodiment of a system of this invention, generally **100**, is shown to include a probe **102** having a tip **104**, which is in proximity to or in contact with a surface tissue **106** over a vein **108** of an underside **109** of a patient's tongue **110**. The system **100** also includes a light delivery subsystem **112** and detection/analysis subsystem **114**. The light delivery subsystem **112** terminates in the probe tip **104** at a light outlet or port **116**, while the detection/analysis subsystem **114** begins in the tip **104** at an output or response signal inlet or port **118**. The light delivery subsystem **112** includes a light source **120** and a light conduit **122** terminating at the light outlet **116**. Preferably, the light conduit is an optical fiber or optical fiber bundle and the light source is a laser or filtered broad spectrum light source (*e.g.*, lamp). The detection/analysis subsystem **114** includes a detector **124**, an analyzer unit **126** and a signal conduit **128** interconnecting the detector **124** and the analyzer **126**. The detector **124** can be located in the tip **104** as shown in **Figure 1A**, in the probe **102** as shown in **Figure 1B** or in the analyzer unit **126** as shown in **Figure 1C**. The output signal forwarded to the analyzer **126** can be optical and/or acoustic, if the detector **124** is located in the analyzer **126** or electrical, if the detector **124** is located in the probe **104**.

[0022] The system **100** works by placing the probe tip **104** in contact with surface tissue **106** over the vein **108**. The light delivery system **112** is then activated, turned on, and excitation radiation travels from the light source **120** through the light conduit **122** and out the light outlet **116** in the probe tip **104**. The excitation radiation then propagates through the surface tissue **106**, a relatively thin tissue layer, and into the vein **108** where a response signal is produced. The response signal then enters the signal port **118** where it is either detected by the detector **124** in the probe **102** or probe tip **104** or travels down the signal conduit **128** to the detector **124** associated with the analyzer unit **126**. The detector **124** converts the signal into a detector response and the analyzer converts the response into a concentration of a blood component and/or a value of a blood parameter.

CHARACTERIZATION OF THE INVENTION

[0023] The present invention is characterized by a method for noninvasive analysis of at least one blood component comprising the steps of:

irradiating blood in a big vein associated with an underside of a patient's tongue with radiation having at least one frequency or wavelength;

detecting a response from blood irradiated in the irradiating step;

calculating a concentration of a blood component, a value of a blood parameter or a mixture or combination thereof.

[0024] The method can also comprise the step of displaying at least one result from the calculating step.

[0025] The present invention is characterized by an apparatus for noninvasive blood analysis comprising:

a probe including a tip having a radiation outlet and a response inlet, where the probe tip is adapted to be placed in proximity to or in contact with a surface of a tissue over a big vein associated with an underside of a patient's tongue;

a light generation/delivery system including a light source capable of generating at least one frequency of light, and a light conduit interconnecting the light source with the radiation outlet, where the system is adapted to deliver radiation to blood in the big vein; and

a detector/analyzer system including a detector adapted to detect a response from the irradiated blood via the response inlet and an analyzer adapted to convert the detected response into a concentration of a blood component and/or a value of a parameter of the blood.

[0026] The apparatus can also include a display adapted to display the response (raw data) or converted response (refined data).

[0027] The above method or apparatus can operate with radiation in the spectral range from about 200 nanometers to about 20 microns.

[0028] The above method and apparatus can utilize use one or a combination of techniques selected from the group consisting of reflectance technique, confocal technique, scanning confocal technique, polarization techniques, interferometry, optoacoustics, low coherence interferometry and reflectometry, techniques based on speckle measurements, fluorescence technique, Raman scatterin technique, and two or multi-photon techniques.

[0029] The above method and apparatus can detect hemoglobin and the radiation comprise wavelengths of about 548 nm, 568 nm, 587 nm, and 805 nm (isosbestic points) and spectral range from about 400 nm to about 640 nm and above about 1120 nm where absorption coefficients of oxy and deoxygenated blood are close to each other.

[0030] The above method and apparatus can detect hematocrit.

[0031] The above method and apparatus can detect hemoglobin and/or glycosylated hemoglobi where the detection and quantitation of hemoglobin and/or glycosylated hemoglobin may be easi

than the detection and quantitation of glucose and cholesterol.

[0032] The above method and apparatus can detect glucose.

[0033] The above method and apparatus can detect cholesterol.

[0034] The above method and apparatus can detect are oxy-hemoglobin, deoxy-hemoglobin, carboxy-hemoglobin.

[0035] The above method and apparatus can detect an exogenous substance.

[0036] The above method and apparatus can detect an exogenous substance selected from the group consisting of a drug, a dye or other reporter in molecular state or a particle made of liquid, gas, or solid material including polymer, metal, semiconductor, dielectric, or a combination of liquid, gas, or solid materials, and a layered structure.

[0037] The above method and apparatus can detect an exogenous substance selected from the group consisting of indocyanine green and Evans blue.

[0038] The above method and apparatus can detect an exogenous substance that are particles with a size from about 0.1 nanometer to about 10 microns.

[0039] The above method and apparatus using microwave radiation.

[0040] The above method and apparatus using radiofrequency radiation.

[0041] The above method and apparatus using ultrasound radiation.

[0042] The above method and apparatus using low-frequency electromagnetic radiation.

[0043] The above method and apparatus using a static electric or magnetic field.

[0044] The above method and apparatus using a hybrid technique for irradiation and detection.

[0045] The above method and apparatus using radiation having one, two, or many wavelength (frequencies).

[0046] All references cited herein are incorporated by reference. While this invention has bee described fully and completely, it should be understood that, within the scope of the appende claims, the invention may be practiced otherwise than as specifically described. Although th invention has been disclosed with reference to its preferred embodiments, from reading th description those of skill in the art may appreciate changes and modification that may be ma which do not depart from the scope and spirit of the invention as described above and claim hereafter.

ABSTRACT

A method for analysis of blood components or parameters is disclosed where a probe having an excitation outlet and a response inlet is placed in proximity to or in contact with a tissue of an underside of a patient's tongue over a big vein in the tongue so that an excitation signal exits the outlet, produces a response which enters the inlet for detection and analysis.

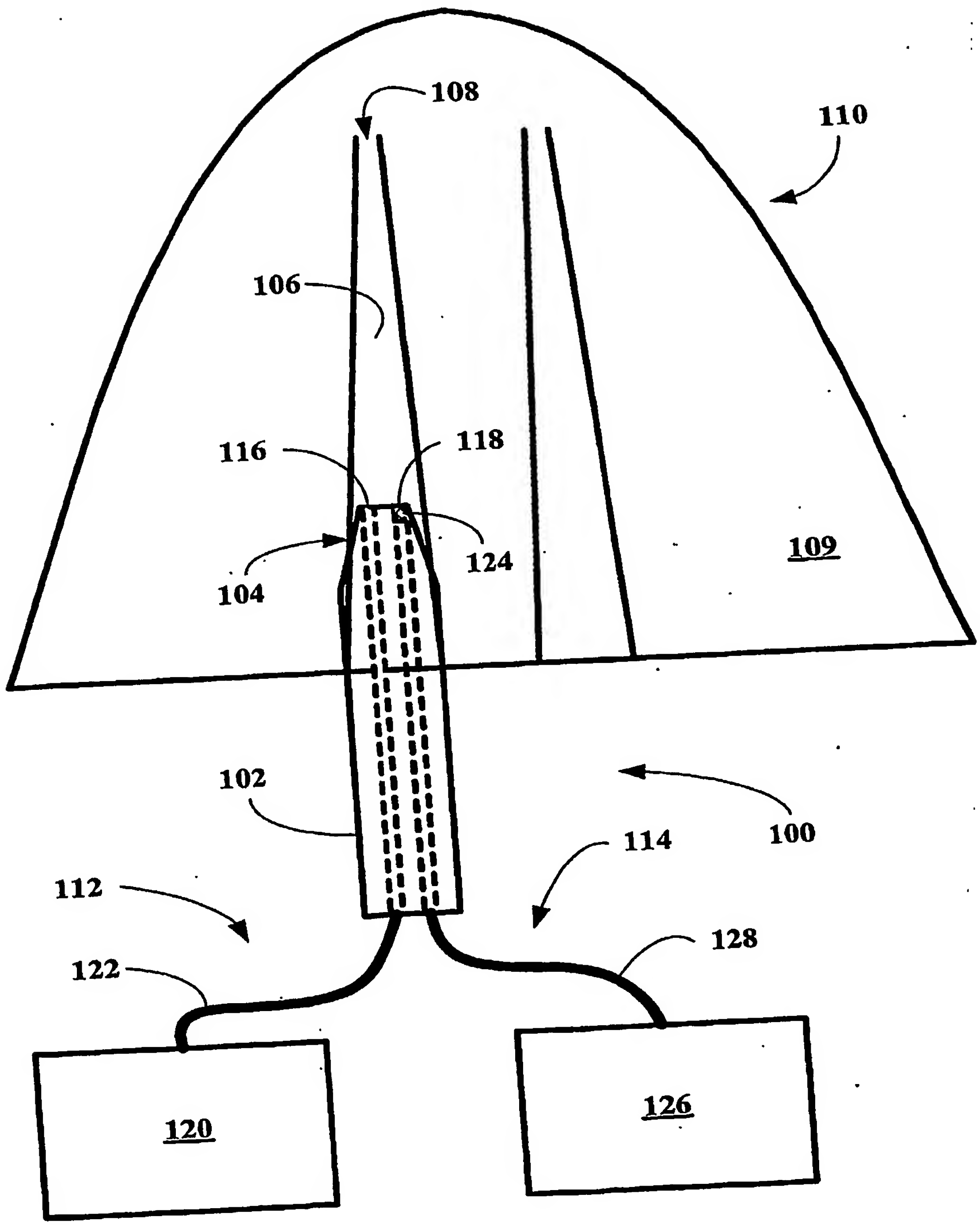

FIG. 1A

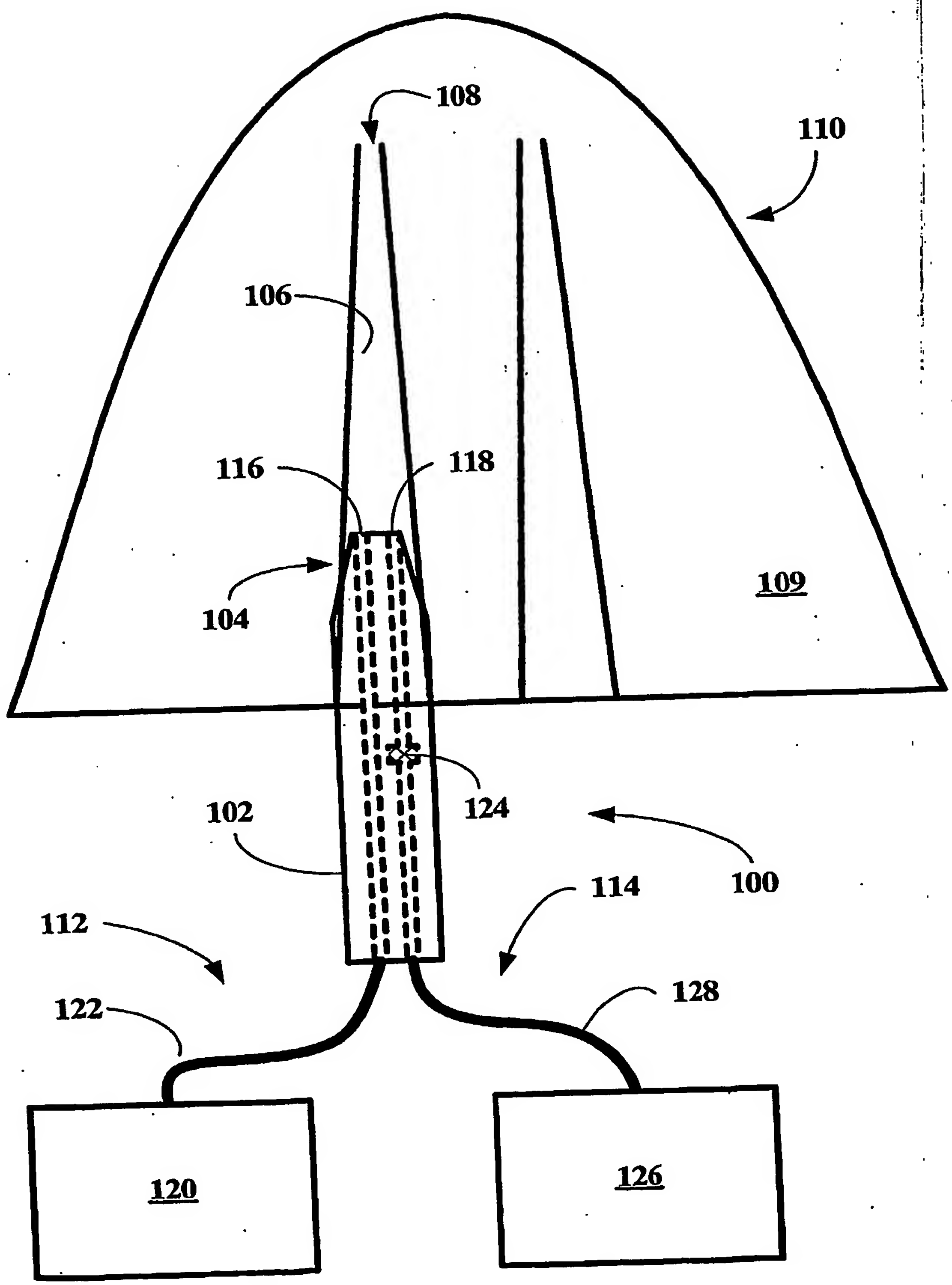

FIG. 1B

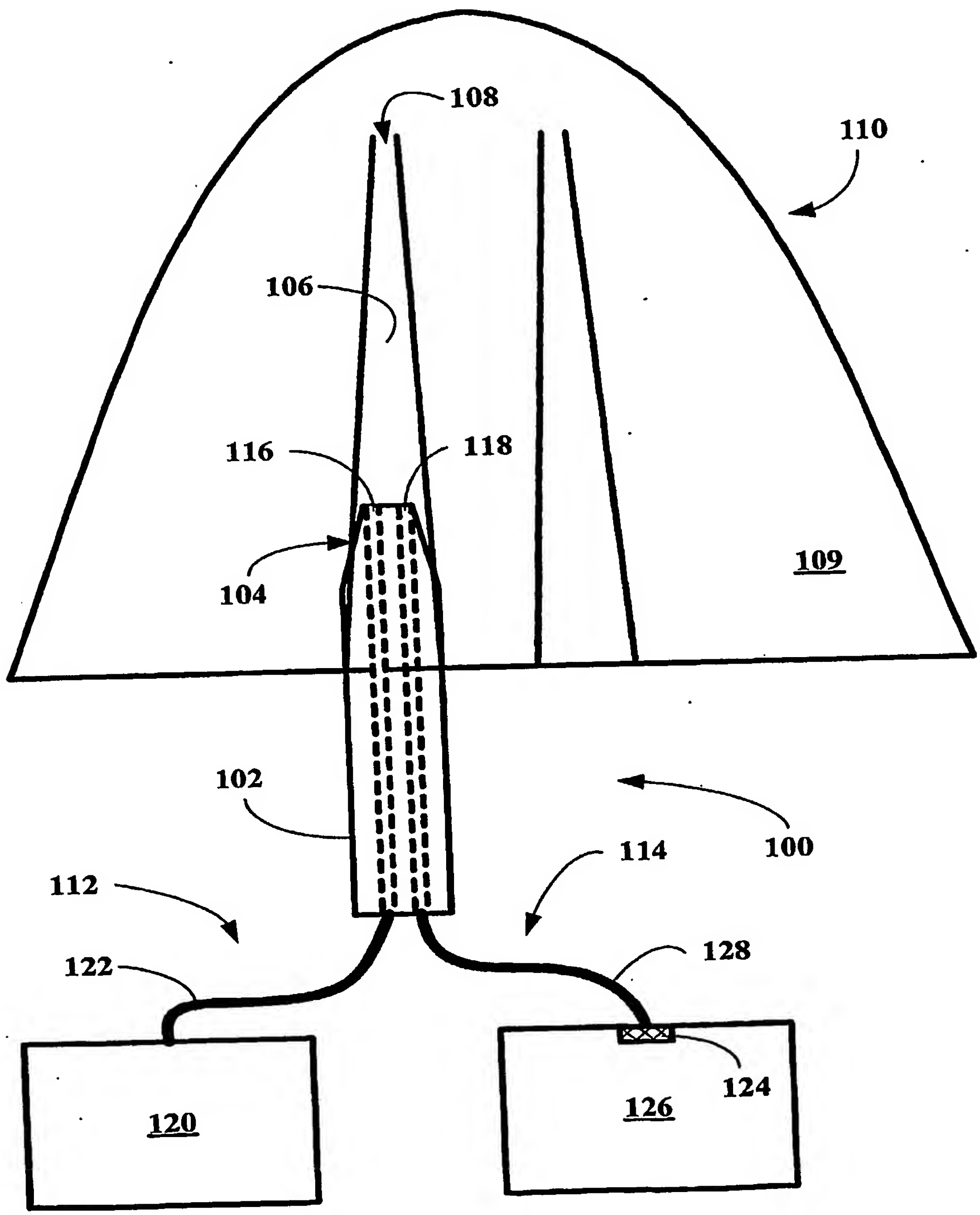

FIG. 1C